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A Study of Systemic Markers of Inflammation in Alcoholic Subjects in the Tertiary Care Centre of Kumaon Region

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Abstract

Introduction: Alcohol is known to contribute to inflammation upon heavy consumption. Inflammation plays an important role in manifestation of numerous diseases. Several systemic biomarkers, through their circulatory levels, may indicate the level of inflammation. However, various epidemiological studies suggest that moderate alcohol intake is associated with lower mortality as compared to abstinence or heavy drinking, primarily due to lowered incidence of vascular accidents. Alcohol drinking has been associated with low grade inflammatory changes which can be depicted as changes in the levels of inflammatory markers, although it has been observed to have anti inflammatory effects when used in moderation.

Materials & Methods: The study population consisted of 100 alcoholic subjects and 50 age and sex matched controls in the age group of 25-60 years. Alcoholic subjects were classified into different categories based on their alcohol consumption in terms of drinks per. Serum high sensitivity C-reactive protein (hs-CRP) and lipoprotein-a (Lp-a) were estimated by turbidimetric immunoassay, serum uric acid was measured by enzymatic(uricase) method and serum albumin was measured by dye binding method (bromocresol purple). Total leucocyte count (TLC) was counted by volumetric impedance method and Wintrobe's method was used for erythrocyte sedimentation rate (ESR) estimation.

Results: The mean serum hs-CRP, serum uric acid, serum Lp-a level and the mean value of ESR were significantly raised ($p < 0.05$) in cases as compared to controls. The mean serum hs-CRP level in the moderate and heavy drinkers was significantly lower($p<0.05$) as compared to occasional and low-moderate drinkers.The mean serum uric acid, serum albumin level and mean value of ESR in moderate and heavy drinkers were

significantly higher ($p<0.05$) as compared to occasional and low-moderate drinkers. In our study, serum hs-CRP levels had significant positive correlation with ESR (0.050; $p<0.05$).

Conclusion: Our study showed significantly low level of biomarkers of inflammation in occasional, low-moderate and moderate drinkers. There was a significant rise in inflammatory markers in heavy alcohol drinking. This suggests a beneficial effect of moderate alcohol intake but a large scale study needs to be done to confirm the above mentioned findings.

Key words: Biomarkers of inflammation, degree of alcohol intake, serum high sensitivity-C reactive protein, serum lipoprotein-(a), serum uric acid, serum albumin, erythrocyte sedimentation rate, total leucocyte count.

Introduction

Alcohol refers to ethyl alcohol or ethanol a volatile liquid derived from fermentation of food stuffs, having formula C_nH_{2n}-OH (R-OH) with hydroxyl group attached to carbon chain. Alcohol has been in social use as a beverage since ages, widely used in various civilizations world over. Alcohol has been associated with dependence potential upon unregulated excessive use, it may even lead to impaired control, resulting in physical compulsions and repeated drinking leading to alcoholism.[1]

Alcoholism is a term of long-standing use and variable meaning, generally taken to refer to chronic continual drinking or periodic consumption of alcohol which is characterized by impaired control over drinking, frequent episodes of intoxication, and preoccupation with alcohol and the use of alcohol despite adverse consequences.[1,3,4] Alcoholic is an individual who suffers from alcoholism. Alcohol dependence is alcohol seeking behavior by an individual despite repeated alcohol related difficulties and its adverse effects.[1,3] It is a serious and advanced form of alcoholism. In absence of dependence alcohol abuse is associated with repeated problems with alcohol in any one of the life areas that include social, interpersonal, legal, occupational problem on repeated use. [1,3]

In India, The National Family Health Survey (2005) reported national prevalence of alcohol use was 4.5%.[2] The unrecorded alcohol consumption in India is estimated to be 1.7 litres pure alcohol per capita for population older than 15years for the years after 1995.[3]

Problem drinking that becomes severe is given the medical diagnosis of “alcohol use disorder” or AUD. AUD is a chronic relapsing brain disease characterized by compulsive alcohol use, loss of control over alcohol intake, and a negative emotional state when not using.[4]

In 2016, the harmful use of alcohol resulted in some 3 million deaths (5.3% of all deaths) worldwide and 132.6 million disability-adjusted life years (DALYs) – i.e. 5.1% of all DALYs in that year.[1] Mortality resulting from alcohol consumption is higher than that caused by diseases such as tuberculosis, HIV/AIDS and diabetes. Among men in 2016, an estimated 2.3 million deaths and 106.5 million DALYs were attributable to the consumption of alcohol. Women experienced 0.7 million deaths and 26.1 million DALYs attributable to alcohol consumption.[1]

Chronic excessive alcohol consumption is considered an important risk factor for diseases of vascular origin like coronary artery diseases (CAD), cerebro-vascular diseases and peripheral vascular diseases. Pro-oxidant effect of ethanol is one of the proposed mechanism responsible for such increased risks.[5,6]

Inflammation plays an important role in manifestation of numerous diseases. Several systemic biomarkers,

through their circulatory levels, may indicate the level of inflammation. Alcohol is known to contribute to inflammation upon heavy consumption. However, various epidemiological studies suggest that the moderate alcohol intake is associated with lower all cause mortality than abstention or heavy drinking, primarily due to lowered risk of vascular accidents. [6, 18-21]

Recently, it has been suggested that moderate alcohol intake decreases the inflammation which may contribute to beneficial effects other than the changes in lipids and haemostatic factors thus reducing overall mortality.[13,14, 18-20] There are some emerging risk factors such as lipoprotein-a (Lp-a), high-senstivity C-reactive protein (hs-CRP), prothrombotic, and proinflammatory factors which are considered to play a pivotal role in the pathogenesis of atherosclerosis.[11]

C-reactive protein (CRP) is an annular (ring-shaped), pentameric protein found in blood plasma, the levels of which rise in response to inflammation.[25] CRP is synthesized by the liver in response to factors released by macrophages and fat cells (adipocytes).[23] It is a member of the pentraxin family of proteins.[24]

High sensitivity C-reactive protein (hs-CRP) is an acute phase marker of inflammation.[18], Observations from prior studies support the hypothesis that CRP is a highly sensitive marker of systemic (micro)-inflammation (atherosclerosis), tissue damage and infection.[23,24]

Lp-a is a low-density lipoprotein (LDL)-like plasma lipoprotein composed of apolipoprotein B (apoB) and a large glycoprotein termed apolipoprotein-a apo(a).[26] Lp-a is the main congenital lipid atherosclerosis risk factor. An Lp-a level above 30mg/dl increases cardiovascular event risk twice, independently of other lipid levels and five times, when LDL level is simultaneously increased.[25,26]

Uric acid (UA) is a product of the metabolism of purine nucleotides that are the principal constituents of cellular energy stores, such as ATP, and components of DNA and RNA. Various epidemiological studies have shown that hyperuricemia is a risk factor for cardiovascular diseases (CVDs) in the general population.[32,33,34]

Albumin is a negative acute phase reactant, also an important contributor to osmotic regulation mechanism as well as transporter of various biomolecule in the body. Alcoholics show marked changes in hematological parameters, hemoglobin and hematocrit values both decrease, while total leukocyte count (TLC) may rise or fall.[13]

Erythrocyte sedimentation rate (ESR) is the rate at which RBCs settle out of plasma under the influence of gravity. The rate at which they settle is measured as the number of millimeters of clear plasma. Erythrocyte sedimentation rate is a non specific biomarker of inflammation. It is not a diagnostic parameter but an indicator of bodily response to tissue injury.[8,13]

The objectives of the present study were to estimate the biomarkers of inflammation - serum high sensitivity C-reactive protein, serum lipoprotein-a, serum albumin, serum uric acid, erythrocyte sedimentation rate (ESR), total leukocyte count (TLC) in alcoholic subjects and their age and sex matched non alcoholic controls, to study the association between the levels of inflammatory biomarkers and the degree of alcohol consumption & to study the correlation between the different parameters of inflammatory markers in alcoholic subjects.

Material and Methods

The present study was carried out in the Department of Biochemistry, in association with the Department of

Medicine, Government Medical College, Haldwani. After informed and written consent, 100 healthy alcoholic subjects free from any acute or chronic illness and 50 age and sex match controls, in the age group of 25-60 years randomly selected from the areas and wards, in and around Haldwani were enrolled in the Medicine OPD of Government Medical College Haldwani.

Smokers, pregnant females, patients on anti-inflammatory drugs and patients suffering from acute and chronic illnesses, and inflammatory diseases were excluded from the study.

All the participants were subjected to detailed history, thorough clinical examination and anthropometric measurements. A detailed history from alcoholic subjects comprising of type of alcoholic beverages consumed, amount, frequency and duration of alcohol consumption was recorded on participant Performa.

Alcoholic subjects were classified into different categories based on their alcohol consumption in terms of drinks per week -

Group I (Occasional Drinkers)	Group II (Low-Moderate Drinkers)	Group III (Moderate Drinkers)	Group IV (Heavy Drinkers)
1-10drink*/Week	10-20drink/Week	20-30drink/Week	>30drink/Week

{*A Standard drink consists of 10-14 gram of ethanol, which is equal to 12 Ounce or 300-360cc of Beer (5-7%), 120-150ml of wine(12%), 30-45ml of hard liquor (40-50% alcohol)}[35]

Taking all aseptic precautions, about 6 ml of blood was drawn by venipuncture from a peripheral vein, with a disposable syringe. All samples were collected in the morning after an overnight fast. Sample for serum hs-CRP, serum lipoprotein-a, serum uric acid, liver function tests and lipid profile, were collected in a plain vial and those for haematological tests in the EDTA vial. The blood samples for haematological tests collected in EDTA vial were tested soon after collection while the blood sample collected in plain vials were allowed to stand for 30 minutes at room temperature for the retraction of clot. It was then centrifuged at 3000 revolutions per minute for 10 minutes to separate the serum. The serum was stored at 4°C in the refrigerator for analysis. Care was taken to avoid haemolysis of samples

Serum high sensitivity C- reactive protein (hs-CRP) and Lipoprotein-a (Lp-a) were estimated by turbidimetric immunoassay using Microlab-300 semiautoanalyzer.

Serum uric acid was measured by enzymatic (uricase) method using cobas (Roche)-501 autoanalyzer.

Serum albumin was measured by dye binding method (bromocresol purple) using cobas (Roche)-501 autoanalyzer.

Total Leucocyte Count (TLC) was counted by volumetric impedance method on Celltac *F* NIHON KOHDEN hematology analyzer.

Erythrocyte Sedimentation Rate (ESR) estimation was done by Wintrobe's method.

Statistical Analysis

The data were compiled and entered in MS Excel sheet and the analysis was carried out using the statistical Package for the Social Sciences (SPSS 19.0.2) for windows. Unpaired t test and Duncan Multiple Range Test (DMRT) were used to analyze the data for statistical significance. Duncan Multiple Range Test was used to show the inter-category significance ($p<0.05$). Different letter superscript indicated significance ($p<0.05$) with each other categories while

that with same letter superscript indicated no significant association (p>0.05) with each other.

Results

Table 1shows the age and sex distribution among cases. 37% of the cases were in the age group 25-33 years followed by 26% within 34-42years, 25% within 43-51 years, 12% within 52-60 years. 87% of the cases were males.

Table 1: Distribution of age and sex among the cases (n=100)

Age group	**Males**		**Females**		**Total**	
(years)	**No**	**%**	**No**	**%**	**No**	**%**
25-33	28	32.18	9	69.23	37	37.00
34-42	23	26.44	3	23.08	26	26.00
43-51	24	27.59	1	7.69	25	25.00
52-60	12	13.79	0	0.00	12	12.00
Total	**87**	**100**	**13**	**100**	**100**	**100**

Table 2 shows the serum levels of Biomarkers of Inflammation in cases and controls. The mean serum hs-CRP level, mean serum uric acid level, mean serum Lp-a level and the mean value of ESR were significantly raised ($p < 0.05$) in cases as compared to the controls.

The mean serum albumin level and the mean value of TLC were not significantly raised ($p > 0.05$) in the cases as compared to controls.

Table 2: Serum levels of Biomarkers of Inflammation in Cases and Controls

Parameter	Cases(n=100) mean ± SD	Controls(n=50)mean ± SD
Serum hs-CRP (mg/dL)	0.334±0.24	0.299*±0.20
Serum uric acid (mg/dL)	5.576±1.81	4.564*±1.48
Serum Lp-a (mg/dL)	24.388±28.19	22.116*±20.13
Serum albumin (g/dl)	4.470±0.70	4.388±0.66
ESR (mm/hr)	14.483±5.15	13.000*± 3.16
TLC (per cubic mm)	6937.68±1983.98	7070.76±2094.43

*significance level as compared to controls: $p < 0.05$

Table 3 shows the serum levels of biomarkers of inflammation in cases according to alcohol intake. The mean serum hs-CRP level in the moderate drinkers (21-30 drinks/week) and heavy drinkers (>30 drinks/week) was significantly lower (p<0.05) as compared occasional drinkers (1-10 drinks/week) and low-moderate drinkers (11-20 drinks/week) respectively, while low-moderate drinkers (11-20 drinks/week) had hs-CRP levels significantly lower (p<0.05) than occasional drinkers (1-10 drinks/week). The mean serum albumin level in the occasional drinkers was significantly (p<0.05) lower as compared to low-moderate, moderate and heavy drinkers.

The mean serum uric acid level in moderate and heavy drinkers was significantly higher (p<0.05) as compared to occasional drinkers and low-moderate drinkers. The mean serum uric acid level in the moderate drinkers was significantly higher as compared to low-moderate drinkers.

The mean serum Lp-a levels and the mean value of TLC did not show any significant (p>0.05) association across different alcoholic groups.

The mean value of ESR in the occasional drinkers was significantly lower ($p<0.05$) as compared to low-moderate, moderate and heavy drinkers.

Table 3: Serum levels of Biomarkers of Inflammation in cases according to alcohol intake

Parameter	Cases			
	1-10drinks/week (n=24)mean ± SD	11- 20 drinks/week (n=34) mean ± SD	21-30 drinks/week (n=20)mean ± SD	>30 drinks/week (n=22)mean ± SD
Serum hs-CRP (mg/dL)	0.393^{a} ± 0.28	0.324^{b} ± 0.19	0.290^{c} ± 0.20	0.290^{c}±0.26
Serum uric acid (mg/dL)	4.75^{b}±1.94	4.94^{b}±1.58	6.7^{a}±1.34	6.72^{a}±1.52
Lp-a (mg/dL)	22.13^{a}±22.19	23.23^{a}±22.88	24.90^{a}±31.25	28.16^{a}±38.43
Albumin (g/dL)	4.12^{b}±0.71	4.40^{a}±0.62	4.55^{a}±0.69	4.78^{a}±0.62
ESR (mm/hr)	13.09^{b}±3.06	14.35^{a}±5.31	14.70^{a}±6.50	16.00^{a}±5.24
TLC (per cmm)	6713.75^{a} ± 1758.185	6947.35^{a} ± 2270.22	6971^{a} ± 1910.963	7136.73^{a} ±1915.12

* Different alphabet superscript show significance ($P<0.05$) with each other and same alphabets indicate no significance ($P>0.05$) with each other.

Fig 2, 3, 4 & 5 show the serum levels of biomarkers of inflammation in cases according to degree of alcohol intake.

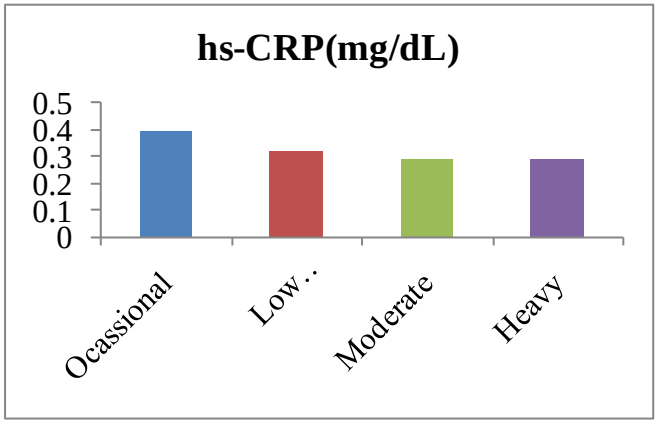

Fig 2: Shows serum levels of hs-CRP in cases according to alcohol intake.

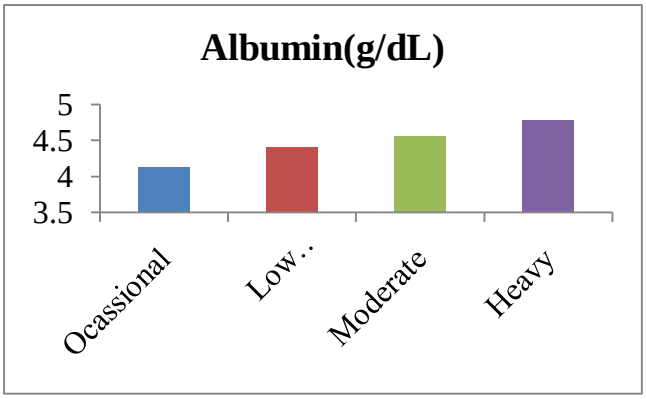

Fig.3: Shows albumin levels in cases according to alcohol intake

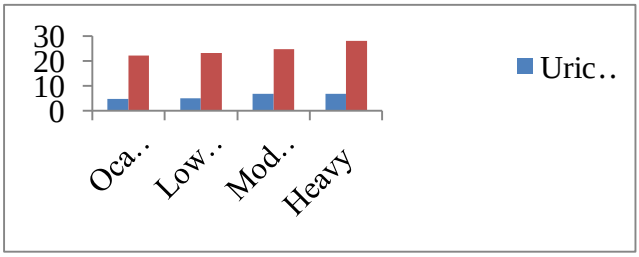

Fig. 4: Shows serum uric acid and Lp-a levels in cases according to alcohol intake.

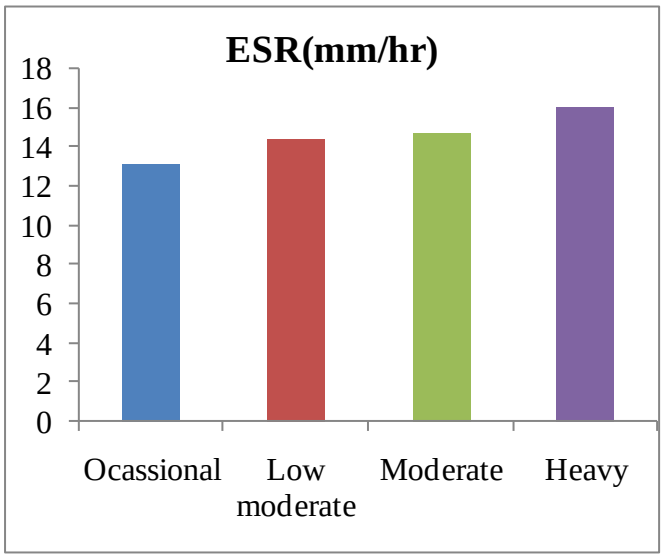

Fig. 5: Shows ESR levels in cases according to alcohol intake.

Table 4: Correlation between hs-CRP with uric acid, albumin, ESR and among cases

	hs-CRP (mg/dL)	Uric acid (mg/dL)	Albumin (g/dL)	ESR (mm/hr)	Lp (a) (mg/dL)	TLC (per cmm)
Correlation coefficient (r)		0.0515	0.0086	0.0502	0.0368	0.0019
S.E.OF 'r'		0.743	0.292	2.121	11.69	838.25
p value		*P<0.05*	*P<0.05*	*P<0.05*	*P>0.05*	*P>0.05*

Table 4 shows that serum levels of hs-CRP had significant negative correlation with uric acid and albumin while it had significant positive correlation with ESR.

Discussion

The use of alcohol beverage is most ancient habit prevalent all over the world and contributes substantially to the global burden of health and social issues. Chronic and acute alcohol intoxication has been attributed to the multitude of diseases like liver cirrhosis, cardiovascular diseases, cancers and neuropsychiatric disorders.[1, 5, 6]

Alcohol consumption is associated with cardiovascular morbidity and mortality in a dose-dependent manner. Although the notion that elevated inflammatory markers increase the risk of cardiovascular disease (CVD) has been increasingly recognized, underlying mechanisms and pathways remain to be elucidated. Specifically, inflammation and dyslipidemia are well established cardiovascular risk factors and closely associated with each other. Moderate alcohol intake has been observed to offer protective effects by decreasing coronary heart disease mortality, while excessive alcohol misuse has been proven detrimental to the cardiovascular system. [5, 6, 18, 21]

In present study the mean serum hs-CRP levels was found to be significantly raised ($p < 0.05$) in cases as compared to the controls **(Table 2),** while comparing between groups according to alcohol intake, the mean serum hs-CRP level in the moderate drinkers and heavy drinkers was significantly lower ($p<0.05$) as compared

occasional drinkers and low-moderate drinkers respectively, while low-moderate drinkers had hs-CRP levels significantly lower ($p<0.05$) than occasional drinkers **(Table 3).**

Imhof *et al.,* [18] have recently reported that there is a U-shaped relation between alcohol intake and C-reactive protein (CRP) with the lowest CRP concentration at alcohol intake of 40–60 g day of ethanol.

Sierksma *et al.,*[20] in a small cross-over study demonstrated a significant reduction of hs-CRP concentrations after 3 weeks of diet- controlled consumption of beer.

Imhof *et al.,* 2001[18]; Stewart *et al.,* 2002[21]; Albert *et al.,* 2003[19]; Volpato *et al.,* 2004[12]; Pai *et al.,* 2006 [14] observed J-shaped associations between alcohol and hs-CRP in both men and women.

Wafika Zarzour, Nada Dehneh, and Mazen Rajab[16] have extensively studied hs-CRP and its association with other biomarkers of inflammation and displayed significant correlations between hsCRP levels and inflammatory markers such as WBC.

In a study conducted by Osei-Bimpong *et.al.,*[17] similar findings between hs-CRP and ESR were observed in a group of healthy males and females, younger than 40 years.

In our study, the mean serum Lp(a) levels was significantly raised ($p < 0.05$) in cases as compared to the controls **(Table 2).** However, the mean serum Lp-a levels in different alcoholic groups did not show any significant ($p>0.05$) association in between them **(Table 3).**

Willeit *et al.,*1995 [42] showed that alcohol drinking was associated with a tendency towards higher Lp (a) levels, but Valimaki e*t al.,* 1993[40], Iso *et al.,* 1996[41]and Paassilta *et al.,* 1998[27] observed a negative correlation between quantity of alcohol intake and Lp-a plasma concentration.

Our study showed hs-CRP had no significant correlation with Lp(a), ($r=0.0368$; $p >0.05$) **(Table 4).** While Ruggiero *et al.,* [28] in a study on patient population found hs-CRP to be strongly correlated to Lp(a). In a study conducted in south Indian population, Lp(a) also correlated well with inflammation linked to the extent and severity of atherosclerosis.

In present study, mean serum uric acid levels in moderate and heavy drinkers was significantly higher ($p<0.05$) as compared to occasional drinkers **(Table 3)**. The mean serum uric acid levels in the moderate drinkers, was significantly higher as compared to low-moderate drinkers.

Bartimaeus *et al.,* 2002 studied effect of alcohol in Uric acid level and found a significant increase in serum Uric acid levels upon regular use.[30]

De Marchi *et al.,* [31] have reported that serum uric acid levels slightly decrease in alcoholic patient due to loss of xanthine oxidase activity in severe hepatocellular injury. Oliveira *et al.,* [43] in their study showed alcohol intake was positively associated with uric acid levels in alcoholics. Ruggiero *et al.,*[28] found a significant positive association between serum levels of uric acid and hs-CRP.

In our study the mean serum albumin level did not show any significant differences in case and controls **(Table 2)**. Danesh J., Collins R. *et al.,* 1998 [37], Danesh J., Peter Whicup *et al.,* 2000[38] in their observation on the effect of alcohol consumption on albumin provided considerable evidence that alcohol exposure alters not only synthesis but also albumin secretion. Arthur J.McCullough, *et al.,*[29] studied alcoholic patient and found serum albumin decreases as synthetic function of the liver declines with advancing

liver diseases. In our study the mean serum albumin level did not show any differences in case and controls.

In present study, the mean ESR levels in cases was found to be significantly ($p < 0.05$) raised as compared to controls **(Table 2)** which is in line with previous studies. Ballard MD[15] from their study suggested that alcohol intake increased the ESR value significantly ($p < 0.05$) in moderate drinkers than abstainers. Arjun Maitra and Chaitali Maitra[22] in a similar study on hematological markers, observed that ESR increased significantly in moderate and high intake group ($p < 0.05$).

In our study mean TLC levels did not show any significant difference ($p > 0.05$) between cases and controls. **(Table2).** Subir K.D. *et al.*, [39] and Latvala J. *et al.*, 2004 [36] observed that moderate alcohol intake had WBC lowering response which was not seen in our study.

Oliveira *et al*., [43] in a study "alcohol intake and effect on inflammatory markers" in Portugal found no significant association was between alcohol intake and leukocyte count which is in line with our study.

Conclusions

Our study demonstrated elevated levels of biomarkers of inflammation in heavy drinkers. It suggests that heavy drinking (>30drinks/week) must be strongly discouraged as it may lead to inflammatory changes.

This study has depicted a significantly lower level of biomarkers of inflammation in low-moderate to moderate alcohol consumption. There was a significant rise in inflammatory markers in heavy alcohol drinking group. The findings of our study concur with other similar studies that there may be some beneficial effects of moderate drinking due to decreased level inflammatory markers.

Screening of all patients of Alcohol Use Disorder (AUD) for biomarkers of inflammation may be a reasonable strategy to diagnose inflammatory diseases in its early stage.

References

1. Global status report on alcohol and health 2018: executive summary. Geneva: World Health Organization; 2018 (WHO/MSD/MSB/18.2). Licence: CC BY-NC-SA 3.0 IGO.
2. National Family Health Survey 1998–1999. India, International Institute for Population Science, 2000. In: WHO Global NCD InfoBase. Geneva, World Health Organization.
3. Alcohol per capita consumption, patterns of drinking and abstention worldwide after 1995. Appendix.2. European Addiction Research, 2001, 7(3):155–157.
4. Kalousova M, Zima T, Popov P, et al. Advanced glycation and end products in patients with chronic alcohol misuse. Alcohol Alcohol 2004; 39:316–20.
5. Averina M, Nilssen O, et al. C-reactive protein and alcohol consumption: Is there a U-shaped association? Results from a population-based study in Russia. The Arkhangelsk study Atherosclerosis 2006; 188: 309–315.
6. O'Keefe JH, Bybee KA, Lavie CJ. (2007) Alcohol and cardiovascular health: the razor-sharp double-edged sword. J Am Coll Cardiol 50:1009–14.
7. The National Family Health Survey 2015-16 (NFHS-4): factsheet of health indicators of Uttrakhand. www.rchiips.org/nfhs-4/factsheet/Uttarakhand.15.10.2018.
8. Thinnahanumaih M, Puranik N,Bidare C, Kammar KF, Venkatakrishniah OK, Maitri V. Moderate alcohol intake for even a short duration has

deleterious effects on hematologic profile in Indian men. Int J Med Sci Public Health 2012; 1:105-108.

9. Klatsky AL. Alcohol and stroke : an epidemiological labyrinth. Stroke 2005; 36:1835-6.
10. Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: An 8-year follow-up of 14 719 initially healthy American women. Circulation 2003;107:391-7
11. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult treatment panel III). JAMA 2001;285:2486‑97.
12. Volpato S, Pahor M, Ferucci L, et al. Relationship of alcohol intake with inflammatory markers and plasminogen activator inhibitor-1 in well functioning older adults. The Health, Aging, and Body Composition Study. Circulation 2004;109:607–12.
13. Nakanishi N, Yoshida H, Okamoto M et al. (2003) Association of alcohol consumption with white blood cell count: a study of Japanese male office workers. J Intern Med 253:367–74.
14. Pai JK, Hankinson SE, Thadhani R et al. (2006) Moderate alcohol consumption and lower levels of inflammatory markers in US men and women. Atherosclerosis 186:113–20.
15. Ballard HS. Hematological complications of alcoholism. Alcoholism: Clinical and Experimental Research. 1989 Sep-Oct;13(5):706–720.
16. A.Osei-Bimpong, J. H. Meek, and S. M. Lewis, “ESR or CRP? A comparison of their clinical utility,” Hematology, vol. 12, no. 4, pp. 353–357, 2007.
17. Wafika Zarzour, Nada Dehneh, and Mazen Rajab. High-Sensitive C-Reactive Protein Levels in a Group of Syrian University Male Students and Its Associations with Smoking, Physical Activity, Anthropometric Measurements, and Some Hematologic Inflammation Biomarkers. International Journal of Inflammation vol.2017 doi.org/10.1155/2017/7
18. Imhof A, Froehlich M, Brenner H, Boeing H, Pepys MB, Koenig W. Effect of alcohol consumption on systemic markers of inflammation. Lancet. 2001;357:763–767.
19. Albert MA, Glynn RJ, Ridker PM. Alcohol consumption and plasma concentration of C-reactive protein. Circulation. 2003;107:443–447.
20. Sierksma A, van der Gaag MS, Kluft C, et al. Moderate alcohol consumption reduces plasma C-reactive protein and fibrinogen levels; a randomized, diet-controlled intervention study. Eur J Clin Nutr. 2002;56: 1130–1136.
21. Stewart SH, Mainous AG III, Gilbert G. Relation between alcohol consumption and C-reactive protein levels in the adult US population. J Am Board Fam Pract. 2002; 15:437–442.
22. Chaitali Maitra, Arjun Maitra Understanding the Pathophysiological Basis of Alterations of Hematological Picture in Alcohol Abuse Patients. Res. Rev.: J. Med. Health Sci . 2015(May – Dec); 3 (4):81-7.
23. Pepys MB, Hirschfield GM (Jun 2003). "C-reactive protein: a critical update". The Journal of Clinical Investigation 111 (12): 1805–12.
24. Lau DC, Dhillon B, Yan H, Szmitko PE, Verma S (May 2005). "Adipokines: molecular links between

obesity and atheroslcerosis". American Journal of Physiology. Heart and Circulatory Physiology 288 (5): H2031–41.

25. Fulcher, G. (1992) Lipoprotein(a): a new independent risk factor or atherosclerosis. Australian and New Zealand Journal of Medicine 22, 326–328.
26. Berg K (1963) A new serum type in man - the Lp-system. Acta Pathol Microbiol Scand 59:369-382.
27. Paassilta, M., Kervinen, K., Rantala, A. O., Savolainen, M. J., Lilja, M., Reunannen, A. and Kesaniemi, Y. A. (1998) Social alcohol consumption and low Lp(a) lipoprotein concentration in middle aged Finnish men: population based study. British Medical Journal 316, 594–595.
28. Ruggiero C, Cherubini A, et al., Uric acid and inflammatory markers. Eur Heart J. 2006 May ; 27(10): 1174–1181.
29. Arthur J. McCullough, M.D., and J. F. Barry O'Cnnor, M.D. A. J. Gastroentrolgy (1998) 93,11.
30. Bartimaeus ES, Eno-Eno M. The effect of alcohol on uric acid level in consumers. Journal of Applied Sciences and Environmental Management. 2002;6(1):7-9.
31. De Marchi S, Cecchin E, Basile A, Bertotti A, Nardini R and Bartoli E (1993) Renal tubular dysfunction in chronic alcohol abuse-effects of abstinence. New England Journal of Medicine 329, 1927-19.
32. Fang J, Alderman MH: Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971–1992. National Health and Nutrition Examination Survey. JAMA 2000, 283(18):2404-2410.
33. Lippi G, Montagnana M, Franchini M, Favaloro EJ & Targher G. The paradoxical relationship between serum uric acid and cardiovascular disease. Clinica Chimica Acta 2008 392 1–7.
34. Strasak A, Ruttmann E, Brant L, Kelleher C, Klenk J, Concin H, Diem G, Pfeiffer K, Ulmer H & the VHM & PP Study Group. Serum uric acid and risk of cardiovascular mortality: a prospective long-term study of 83, 683 Austrian men. Clinical Chemistry 2008 54 273–284.
35. www.niaaa.gov.in/youth drinking guidelines; 20.10.2017.
36. Latvala J, Parkkila S, Niemelä O. Excess alcohol consumption is common in patients with cytopenia: studies in blood and bone marrow cells. Alcohol Clin Exp Res 2004; 28:619–24
37. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA 1998; 279: 1477–82.
38. Danesh J, Whincup P, Walker M, et al. Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses. BMJ 2000; 321: 199–204.
39. Subir KD and Vasudevan DM. Biochemical diagnosis of alcoholism. IJCB. 2005; 20(1):35-42.
40. Valimaki, M., Kahri, J., Laitinen, K., Lahdenpera, S., Kuusi, T., Ehnholms, C., Jauhiainen, M., Bard, M., Fruchart, J. C. and Taskinen, M.-R. (1993) High density lipoprotein subfractions, apolipoprotein A-I containing lipoproteins, lipoprotein (a), and cholesteryl ester transfer protein activity in alcoholic women before and after ethanol withdrawal. European Journal of Clinical Investigation.doi.org/10.111/j.1365-2362.

41. Iso, H., Koike, K. A., Folsom, A. R., Shimamoto, T., Sato, S., Lida, M. and Komachi, Y. (1996) Lipoprotein(a) and its correlates in Japanese and U.S. population samples. Annals of Epidemiology 6, 324–330.
42. Willeit, J., Kiechl, S., Santer, P., Oberhollenzer, F., Egger, G., Jarosch, E. and Mair, A. (1995) Lipoprotein(a) and asymptomatic carotid artery disease. Evidence of prominent role in the evolution of advanced carotid plaques: The Bruneck Study. Stroke 26, 1582–1587.
43. Andreia Oliveira, Fernando Rodríguez-Artalejo and Carla Lopes. Alcohol Intake and Systemic Markers of Inflammation—Shape of the Association According to Sex and Body Mass Index Alcohol & Alcoholism Vol. 45, No. 2, pp. 119–125, 2010.